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THE LABORATORY OF THE LIVING ORGANISM

By Dr. M. O. FORSTER, F.R.S.

PRESIDENT OF THE CHEMICAL SECTION

AMONGST the many sources of pleasure to be found in contemplating the wonders of the universe, and denied to those untrained in scientific principles, is an appreciation of infra-minute quantities of matter. It may be urged by some that within the limits of vision imposed by telescope and microscope, ample material exists to satisfy the curiosity of all reasonable people, but the appetite of scientific inquiry is insatiable, and chemistry alone, organic, inorganic, and physical, offers an instrument by which the investigation of basal changes may be carried to regions beyond those encompassed by the astronomer and the microscopist.

It is not within the purpose of this address to survey that revolution which is now taking place in the conception of atomic structure; contributions to this question will be made in our later proceedings and will be followed with deep interest by all members of the section. Fortunately for our mental balance the discoveries of the current century, whilst profoundly modifying the atomic imagery inherited from our predecessors, have not yet seriously disturbed the principles underlying systematic organic chemistry; but they emphasise in a forcible manner the intimate connection between different branches of science, because it is from the mathematical physicist that these new ideas have sprung. Their immediate value is to reaffirm the outstanding importance of borderline research and to stimulate interest in sub-microscopic matter.

This interest presents itself to the chemist very early in life and dominates his operations with such insistence as to become axiomatic. So much so that he regards the universe as a vast theatre in which atomic and molecular units assemble and interplay, the resulting patterns into which they fall depending on the physical conditions imposed by nature. This enables him to regard micro-organisms as co-practitioners of his craft, and the chemical achievements of these humble agents have continued to excite his admiration since they were revealed by Pasteur. The sixty years which have now elapsed are rich in contributions to that knowledge which comprises the science of micro-biochemistry, and in this province, as in so many others, we have to deplore the fact that the principal advances have been made in countries other than our own. On this ground, fortified by the intimate relation of the science to a number of important industries, A. Chaston Chapman, in a series of illuminating and attractive Cantor Lectures in December, 1920, iterated his plea of the previous year for the foundation of a National Institute of Industrial Micro-biology, whilst H. E. Armstrong, in Birmingham a few weeks later, addressed an appeal to the brewing industry, which, although taking the form of a memorial lecture, is endowed with many lively features depicting in characteristic form the manner in which the problems of brewing chemistry should, in his opinion, be attacked.

Lamenting as we now do so bitterly the accompaniments and consequences of war, it is but natural to snatch at the slender compensations which it offers, and not the least among these must be recognised the stimulus which it gives to scientific inquiry. Pasteur's *Etudes sur la Bière* were inspired by the misfortunes which overtook his country in 1870-71, and the now well-known process of Connstein and Lüdecke for augmenting the production of glycerol from glucose was engendered by parallel circumstances. That acquaintance with the yeast-cell which was an outcome of the former event had, by the time of the latter discovery, ripened into a firm friendship, and those who slander the chemical activities of this genial fungus are defaming a potential benefactor. Equally culpable are those who ignore them. If children were encouraged to cherish the same intelligent sympathy with yeast-cells which they so willingly display towards domestic animals and silkworms, perhaps there would be fewer crazy dervishes to deny us the moderate use of honest malt-liquors and unsophisticated wines, fewer pitiable maniacs to complicate our social problems by habitual excess.

Exactly how the cell accomplishes its great adventure remains a puzzle, but many parts of the machinery have already been recognised. Proceeding from the discovery of zymase (1897), with passing reference to the support thus given by Buchner to Liebig's view of fermentation, Chapman emphasises the importance of contributions to the subject by Harden and W. J. Young, first in revealing the dual nature of zymase and the distinctive properties of its co-enzyme (1904), next in recognising the acceleration and total increase in fermentation produced by phosphates, consequent on the formation of a hexosediphosphate (1908).

In this connection it will be remembered that a pentose-phosphate is common to the four nucleotides from which yeast nucleic acid is elaborated. The stimulating effect developed by phosphates would not be operative if the cell were not provided with an instrument for hydrolysing the hexose-diphosphate as produced, and this is believed by Harden to be supplied in the form of an enzyme, hexosephosphatase, the operation of which completes a cycle. As to the stages of disruption which precede the appearance of alcohol and carbon dioxide, that marked by pyruvic acid is the one which is now most favoured. The transformation of pyruvic acid into acetaldehyde and carbon dioxide under the influence of a carboxylase, followed by the hydrogenation of aldehyde to alcohol, is a more acceptable course than any alternative based upon lactic acid. Moreover, Fernbach and Schoen (1920) have confirmed their previous demonstration (1914) of pyruvic acid formation by yeast during alcoholic fermentation.

The strict definition of chemical tasks allotted to yeasts, moulds, and bacteria suggests an elaborate system of microbial trades-unionism. E. C. Grey (1918) found that *Bacillus coli communis* will, in presence of calcium carbonate, completely ferment forty times its own weight of glucose in forty-eight hours, and later (1920) exhibited the threefold character of the changes involved which produce (1) lactic acid, (2) alcohol with acetic and succinic acids, (3) formic acid, carbon dioxide, and hydrogen. Still more recent extension of this inquiry by Grey and E. G. Young (1921) has shown that the course of such changes will depend on the previous experience of the microbe. When its immediate past history is anærobic, fermentation under anærobic conditions yields very little or no lactic acid and greatly diminishes the production of succinic acid, whilst acetic acid appears in its place; admission of oxygen during fermentation increases the formation of lactic, acetic, and succinic acids, diminishes the formation of hydrogen, carbon dioxide, and formic acid, but leaves the quantity of alcohol unchanged. The well-known oxidising effect of *Aspergillus niger* has been shown by J. N. Currie (1917) to proceed in three stages marked by citric acid, oxalic acid, and carbon dioxide, whilst Wehmer (1918) has described the condition under which citric acid and, principally, fumaric acid are produced by *Aspergillus fumaricus*, a mould also requiring oxygen for its purpose. The lactic bacteria are a numerous family and resemble those producing acetic acid in their venerable record of service to mankind, whilst among the most interesting of the parvenus are those responsible for the conversion of starch into butyl alcohol and acetone. Although preceded by Schardinger (1905), who discovered the ability of B. *macerans* to produce acetone with acetic and formic acids, but does not appear to have pursued the matter further, the process associated with the name of A. Fernbach, and the various modifications which have been introduced during the past ten years are those best known in this country, primarily because of the anticipated connection with synthetic rubber, and latterly on account of the acetone famine arising from the War. The King's Lynn factory was resuscitated and arrangements had just been completed for adapting spirit distilleries to application of the process when, owing to the shortage of raw material in 1916, operations were transferred to Canada and ultimately attained great success in the factory of British Acetones, Toronto.

Much illuminating material is to be found in the literature of 1919-20 dealing with this question in its technological and bacteriological aspects. Ingenuity has been displayed in attempting to explain the chemical mechanism of the process, the net result of which is to produce roughly twice as much butyl alcohol as acetone. The fermentation itself is preceded by saccharification of the starch, and in this respect the bacteria resemble those moulds which have lately been brought into the technical operation of starch-conversion, especially in

France. The amyloclastic property of certain moulds has been known from very early times, but its application to spirit manufacture is of recent growth and underlies the amylo-process which substitutes *Mucor Boulard* for malt in effecting saccharification. Further improvement on this procedure is claimed for *B. mesentericus,* which acts with great rapidity on grain which has been soaked in dilute alkali; it has the advantage of inferior proteolytic effect, thus diminishing the waste of nitrogenous matter in the raw material.

Reviewing all these circumstances we find that, just as the ranks of trades-union labour comprise every kind of handicraftsman, the practitioners of micro-biochemistry are divisible into producers of hydrogen, carbon dioxide, formic acid, acetaldehyde, ethyl alcohol, acetic, oxalic, and fumaric acids, acetone, dihydroxyacetone, glycerol, pyruvic, lactic, succinic and citric acids, butyl alcohol, butyric acid. Exhibiting somewhat greater elasticity in respect of overlapping tasks, they nevertheless go on strike if underfed or dissatisfied with their conditions; on the other hand, with sufficient nourishment and an agreeable temperature, these micro-trades-unionists display the unusual merit of working for twenty-four hours a day. One thing, however, they have consistently refused to do. Following his comparison of natural and synthetic monosaccharides towards different families of yeast (1894), Fischer and others have attempted to beguile unsuspecting microbes into acceptance of molecules which do not harmonise with their own enzymic asymmetry. Various *apéritifs* have been administered by skilled *chefs de cuisine,* but hitherto the little fellows have remained obdurate.

Beyond a placid acceptance of the more obvious benefits of sunshine, the great majority of educated people have no real conception of the sun's contribution to their existence. What proportion of those who daily use the metropolitan system of tube-railways, for instance, could trace the connection between their progress and the sun? Very moderate instruction comprising the elements of chemistry and energy would enable most of us to apprehend this modern wonder, contemplation of which might help to alleviate the distresses and exasperation of the crush-hours.

For many years past, the problem connected with solar influence which has most intrigued the chemist is to unfold the mechanism enabling green plants to assimilate nitrogen and carbon. Although atmospheric nitrogen has long been recognised as the ultimate supply of that element from which phyto-protoplasm is constructed, modern investigation has indicated as necessary a stage involving association of combined nitrogen with the soil prior to absorption of nitrogen compounds by the roots, with or without bacterial cooperation. Concurrently, the agency by which green plants assimilate carbon is believed to be chlorophyll, operating under solar influence by some such mechanism as has been indicated in a preceding section.

Somewhat revolutionary views on these two points have lately been expressed by Benjamin Moore, and require the strictest examination, not merely owing to the fundamental importance of an accurate solution being reached, but also on account of the stimulating and engaging manner in which he presents the problem. Unusual psychological features have been introduced. Moore's 'Biochemistry,' published three months ago, will be read attentively by many chemists, but the clarity of presentation and the happy sense of conviction which pervade its pages must not be allowed to deter independent inquirers from confirming or modifying his conclusions. The book assumes a novel biochemical aspect by describing the life-history of a research. The first two chapters, written before the experiments were begun, suggest the conditions in which the birth of life may have occurred, whilst their successors describe experiments which were conducted as a test of the speculations and are already receiving critical attention from others (e.g., Baly, Heilbron and Barker, Transactions of the Chemical Society, 1921, p. 1025).

It is with these experiments that we are, at the moment, most concerned. The earliest were directed toward the synthesis of simple organic materials by a transformation of light energy under the influence of inorganic colloids, and indicated that formaldehyde is produced when carbon dioxide passes into uranium or ferric hydroxide sols exposed to sunlight or the mercury arc lamp. Moore then declares that, although since the days of de Saussure (1804) chlorophyll has been regarded as the fundamental agent in the photosynthesis of living matter, there is no experimental evidence that the primary agent may not be contained in the colourless part of the chloroplast, chlorophyll thus being the result of a later synthetic stage. 'The function of the chlorophyll may be a protective one to the chloroplast when exposed to light, it may be a light screen as has been suggested by Pringsheim, or it may be concerned in condensations and polymerisations subsequent to the first act of synthesis with production of formaldehyde' (p. 55). In this connection it is significant that chlorosis of green plants will follow a deficiency of iron even in presence of sunlight (Molisch, 1892), and that a development of chlorophyll can be restored by supplying this deficiency, although iron is not a component of the chlorophyll molecule; moreover, green leaves etiolated by darkness and then exposed to light regain their chlorophyll, which is therefore itself a product arising from photosynthesis.

H. Thiele (1907) recorded the swift conversion of nitrate into nitrite by the rays from a mercury quartz lamp, whilst O. Baudisch (1910) observed that daylight effects the same change, and from allied observations was led (1911) to conclude that assimilation of nitrate and nitrite by green plants is a photochemical process. Moore found (1918) that in solutions of nitrate undergoing this reduction green leaves check the accumulation of nitrite, indicating their capacity to absorb the more active compound. Proceeding from the hypothesis that one of the organisms arising earliest in the course of evolution must have possessed, united in a single cell, the dual function of assimilating both carbon and nitrogen, he inquired (1918) whether the simplest unicellular algæ may not also have this power. He satisfied himself that in absence of all sources of nitrogen excepting atmospheric, and in presence of carbon dioxide, the unicellular algæ can fix nitrogen, grow and form proteins by transformation of light energy; the rate of growth is accelerated by the presence of nitrites or oxides of nitrogen, the latter being supplied in gaseous form by the atmosphere. From experiments (1919) with green seaweed (*Enteromorpha compressus*), Moore concluded also that marine algæ assimilate carbon from the bicarbonates of calcium and magnesium present in sea-water, which thereby increases in alkalinity, and further convinced himself that the only source of nitrogen available to such growth is the atmosphere. A description of these experiments, which were carried out in conjunction with E. Whitley and T. A. Webster, has appeared also in the Proceedings of the Royal Society (1920 and 1921).

For the purpose of distinguishing between (1) the obsolete view of a vital force disconnected with such forms of energy as are exhibited by non-living transformers and (2) the existence in living cells of only such energy forms as are encountered in non-living systems, Moore uses the expression 'biotic energy' to represent that form of energy peculiar to living matter. 'The conception, in brief, is that biotic energy is just as closely, and no more, related to the various forms of energy existing apart from life, as these are to one another, and that in presence of the proper and adapted energy transformer, the living cell, it is capable of being formed from or converted into various of these other forms of energy, the law of conservation of energy being obeyed in the process just as it would be if an exchange were taking place between any two or more of the inorganic forms' (p. 128). The most characteristic feature of biotic energy, distinguishing it from all other forms, is the power which it confers upon the specialised transformer to proliferate.

In 'The Salvaging of Civilisation,' H. G. Wells has lately directed the attention of thoughtful people to the imperative need of reconstructing our outlook on life. Convinced that the state-motive which, throughout history, has intensified the self-motive must be replaced by a world-motive if the whole fabric of civilisation is not to crumble in ruins, he endeavours to substitute for a League of Nations the conception of a World State. In the judgment of many quite benevolent critics his essay in abstract thought lacks practical value because it underestimates the combative selfishness of individuals. Try to disguise it as one may, this quality is the one which has enabled men to emerge from savagery, to build up that most wonderful system of colonial organisation, the Roman Empire, and to shake off the barbaric lethargy which engulfed Europe in the centuries following the fall of Rome. The real problem is how to harness this combative selfishness. To eradicate it seems impossible, and it has never been difficult to find glaring examples of its insistence among the apostles of eradication. Why cry for the moon? Is it not wiser to recognise this quality as an inherent human characteristic, and whether we brand it as a vice or applaud it as a virtue endeavour to bend it to the elevation of mankind? For it could so be bent. Nature ignored or misunderstood is the enemy of man; nature studied and controlled is his friend. If the attacking force of this combative selfishness could be directed, not towards the perpetuation of quarrels between different races of mankind, but against nature, a limitless field for patience, industry, ingenuity, imagination, scholarship, aggressiveness, rivalry, and acquisitiveness would present itself; a field in which the disappointment of baffled effort would not need to seek revenge in the destruction of our fellow-creatures: a field in which the profit from successful enterprise would automatically spread through all the communities. Surely it is the nature-motive, as distinct from the state-motive or the world-motive, which alone can salvage civilisation.

Before long, as history counts time, dire necessity will have impelled mankind to some such course. Already the straws are giving their proverbial indication. The demand for wheat by increasing populations, the rapidly diminishing supplies of timber, the wasteful ravages of insect pests, the less obvious, but more insidious depredations of our microscopic enemies, and the blood-curdling fact that a day must dawn when the last ton of coal and the last gallon of oil have been consumed, are all circumstances which, at present recognised by a small number of individuals comprising the scientific community, must inevitably thrust themselves upon mankind collectively. In the campaign which then will follow, chemistry must occupy a prominent place because it is this branch of science which deals with matter more intimately than any other, revealing its properties, its transformations, its application to existing needs, and its response to new demands. Yet the majority of our people are denied the elements of chemistry in their training, and thus grow to manhood without the slightest real understanding of their bodily processes and composition, of the wizardry by which living things contribute to their nourishment and to their æsthetic enjoyment of life.

It should not be impossible to bring into the general scheme of secondary education a sufficiency of chemical, physical, mechanical, and biological principles to render every boy and girl of sixteen possessing average intelligence at least accessible to an explanation of modern discoveries. One fallacy of the present system is to assume that relative proficiency in the inorganic branch must be attained before approaching organic chemistry. From the standpoint of correlating scholastic knowledge with the common experiences and contacts of daily life this is quite illogical; from baby's milk to grandpa's Glaxo the most important things are organic, excepting water. Food (meat, carbohydrate, fat), clothes (cotton, silk, linen, wool), and shelter (wood) are organic, and the symbols for carbon, hydrogen, oxygen and nitrogen can be made the basis of skeleton representations of many fundamental things which happen to us in our daily lives without first explaining their position in the periodic table of all the elements. The curse of mankind is not labour, but waste; misdirection of time, of material, of opportunity, of humanity.

Realisation of such an ideal would people the ordered communities with a public alive to the verities, as distinct from irrelevancies of life, and apprehensive of the ultimate danger with which civilization is threatened. It would inoculate that public with a germ of the nature-motive, producing a condition which would reflect itself ultimately upon those entrusted with government. It would provide the mental and sympathetic background upon which the future truthseeker must work, long before he is implored by a terrified and despairing people to provide them with food and energy. Finally, it would give an unsuspected meaning and an unimagined grace to a hundred commonplace experiences. The quivering glint of massed bluebells in broken sunshine, the joyous radiance of young beech-leaves against the stately cedar, the perfume of hawthorn in the twilight, the florid majesty of rhododendron, the fragrant simplicity of lilac; periodically gladden the most careless heart and the least reverent spirit; but to the chemist they breathe an added message, the assurance that a new season of refreshment has dawned upon the world, and that those delicate syntheses, into the mystery of which it is his happy privilege to penetrate, once again are working their inimitable miracles in the laboratory of the living organism.

EXPERIMENTAL GEOLOGY

By Dr. J. S. FLETT, F.R.S.

PRESIDENT OF THE GEOLOGICAL SECTION

AMONG the citizens of Edinburgh in the closing years of the eighteenth century there was a brilliant little group of scientific, literary, and philosophical writers. These were the men who founded the Royal Society of Edinburgh in the year 1783, and many of their important papers appear in the early volumes of its Transactions. Among them were Adam Ferguson, the historian and philosopher; Black, the chemist who discovered carbonic acid and the latent heat of water; Hope, who proved the expansion of water on cooling; Clerk of Eldin, who made valuable advances in the theory of naval tactics, and his brother, Sir George Clerk; Hutton, the founder of modern geology;